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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: February 10, 2003

SUBJECT: Ziram: HED Risk Assessment for the Reregistration Eligibility Decision (RED) Document.
PC Code: 034805 Reregistration Case # 2180
DP Barcode, D288031
Submission Barcode S621041

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Attached is HED's revised risk assessment for the fungicide, Ziram (also known as Zinc dimethyldithiocarbamate) for purposes of issuing a Reregistration Eligibility Decision (RED) Document. This document updates the January 29, 2002 version of the Risk Assessment by incorporating responses to additional public comments. The HED Cancer Assessment Review Committee (CARC) met to consider newly submitted information and issued a revised CARC report in response to public comment. A cumulative risk assessment considering risks from other pesticides or chemical compounds having a common mechanism of toxicity is not included in this assessment because HED has not yet determined if there are any other chemical substances that have a mechanism of toxicity common with that of ziram. The disciplinary science chapters and other supporting documents are included as appendices as follows:

Use Closure Memo. Laura Parsons (6/22/01)
Report of the Hazard Identification Assessment Review Committee. David Nixon (09/25/01, 014681)
Report of the Cancer Assessment Review Committee. Jessica Kidwell (02/06/03, TXR 0051541)
Report of the FQPA Safety Factor Committee. Brenda Tarplee (09/19/01, 014675)
Report of the Metabolism Assessment Review Committee. Gary Otakie (12/16/99, D261844)
Product and Residue Chemistry Chapter. Gary Otakie (01/17/02, D280352.)
Toxicology Chapter. Sanjivani Diwan, (09/25/01, D277421)*
Occupational and Residential Exposure Assessment. Timothy Leighton (09/12/01, D276785)*
Anticipated Residues, Acute, Chronic, and Cancer Dietary Exposure and Risk Analyses.
Thurston Morton (01/16/2002, D280195.)*
Review of Incident Reports. J. Blondell and M. Spann (08/10/01, D276936)
Tier II Surface Drinking Water assessment. Faruque Khan (1/24/02, D280450)*

* Note: Based on the 12/04/02 re-evaluation of the carcinogenic potential of ziram by HED's Cancer Assessment Review Committee (CARC), assessments of cancer risk provided in these* science chapters are no longer applicable.

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1.0 EXECUTIVE SUMMARY

Ziram (Zinc dimethyldithiocarbamate), is a dimethyldithiocarbamate fungicide used to control fungal diseases on stone fruits, pome fruits, nut crops, vegetables and ornamentals. It is used to prevent crop damage in the field and is also applied prior to harvesting in order to prevent fruits from deterioration in storage or transport. Additionally ziram is used as a preservative in adhesives, caulks, sealants, wallboard, and in exterior latex paint (in-can-preservative). It is also registered for residential use as a rabbit repellent on outdoor ornamentals.

About 20-26 million pounds of ziram per year are used on approximately 500,000 acres of cropland. Approximately 26% is used on pears, 20% on almonds, 19% on apricots and 13% on nectarines. For the rest of the sites usage is approximately 22%. Application rates range from 1.52 lb ai/acre on ornamentals up to 6.08 lb ai/acre for growing agricultural crops (dormant peach rate of 7.6 lb ai/acre). Antimicrobial use rates are from 0.185 to 0.5 percent in adhesives and wallboard, and up to 3 percent in paints. The Ziram Task Force consists of Cerexagri, Inc. (formerly Elf Atochem, Inc.), UCB Chemicals, and R.T. Vanderbilt Co, Inc. Four other registrants who purchase their technical from Task Force Members are: Gowan Company, Drexel Chemical Company, Platte Chemical Company and Bonide Products. Ziram is available as dry flowable, wettable powder and liquid formulations. Applications of ziram include dormant and foliar treatments. Antimicrobial uses of ziram are restricted for industrial use only (EPA Reg No. 1965-79). Ziram may be applied by groundboom, aerial, and airblast sprayers along with hand-held equipment for ornamental uses. For other specialty uses (i.e. rabbit repellent), applications may be made using hand-held equipment.

Ziram is a List B reregistration pesticide. The Agency has identified newer exposure and some toxicity data pertaining to ziram that have become available since the Phase 4 Review and Data Call-In (DCI) Notice were issued in 1991. In addition, the Agency has recently re-evaluated the toxicology and exposure databases for ziram to make a determination of potential increased susceptibility of infants and children, as mandated by the Food Quality Protection Act of 1996 (FQPA). The Agency has performed refined dietary, occupational and residential exposure assessments for ziram with new information and new methodologies that were previously unavailable.

The toxicology database for ziram is largely complete with respect to the OPPTS Guideline requirements with the exception of data gaps for morphometric analyses of brain tissues and statistical analyses of the neurobehavioral data gathered in the developmental neurotoxicity study, a dominant lethal study, a 28-day inhalation study, and a metabolite identification study in rats. The results of acute toxicity studies indicate that ziram is a severe eye irritant, exhibits moderate acute toxicity via the oral and inhalation routes and low toxicity via the dermal route. It is not irritating to the skin and is a moderate dermal sensitizer.

The mechanism of ziram-induced toxicity has not been fully investigated. The primary target organs of ziram appear to be the nervous system, liver, and thyroid. A single oral dose causes neurological impairments (ataxia and impaired gait) while repeated short term exposure results in inhibition of brain cholinesterase and brain neurotoxic esterase in rats. Liver histopathology, sometimes accompanied by increases in hepatic serum enzyme levels, was seen at various doses in the rat subchronic and chronic studies and the mouse carcinogenicity study. When administered orally, ziram is rapidly absorbed, distributed, and excreted within 72 hours with a negligible amount being distributed throughout the body. The tissue distribution and excretion data suggests minimal dermal absorption. Long-term dietary administration of ziram resulted in an increased incidence of thyroid C-cell hyperplasia, thyroid C-cell tumors and benign hemangiomas in male rats and pulmonary alveolar/bronchiolar tumors in female mice. On December 5, 2002, the Cancer Assessment Review Committee (CARC) re-evaluated the carcinogenic potential of ziram to incorporate newly received information. In accordance with the Agency's *Draft*

Guidelines for Cancer Risk Assessment (July, 1999), the CARC reclassified ziram into the category “Suggestive of carcinogenicity to humans” based on the occurrence of hemangiomas and, possibly, preputial gland adenomas in male CD and F344 rats, respectively. The Committee further recommended that no quantification of human carcinogenic risk be determined for Ziram. In addition, the Committee determined that no conclusion can be reached regarding the potential of ziram to induce chromosome aberrations in the whole animal. Based on the acceptable *in vitro* data with purified ziram, an *in vivo* concern is not apparent. This is supported by the evidence showing positive results but only when the purity of ziram is <90% or not known. Since test material purity has become a major issue regarding mammalian cell genotoxicity and carcinogenicity, it should not be ignored for the *in vivo* genetic toxicology data. Based on these considerations, it is concluded that ziram consistently induces gene mutations in *Salmonella typhimurium*, however, this finding is not predictive of carcinogenesis since noncarcinogenic dimethyldithiocarbamates are also positive for gene mutations in *S. typhimurium*. In its previous report (S. Diwan, 4/6/00, HED Doc. No. 014681) the CARC, recommended that a dominant lethal assay be conducted to address a possible concern for heritable effects. However, when the *in vivo* data were revisited, it was found that there was no information in the published studies regarding the purity of the ziram samples and that the studies were compromised by other serious deficiencies. Consequently, the request for a dominant lethal assay is no longer justified. The available acceptable studies satisfy the pre-1991 test guidelines for mutagenicity.

The doses used to assess hazards for various exposure scenarios include chronic dietary reference doses (RfDs), and short-, intermediate- and long-term dermal and inhalation no observable adverse effect levels (NOAELs). The toxicity endpoint (clinical signs) for the acute dietary risk to the general population and various population subgroups is based on the lowest observed adverse effect level (LOAEL) from an acute oral neurotoxicity study in rats. Increased incidence of resorptions and postimplantation loss in developmental rabbit study was the endpoint selected for short-term dermal and inhalation occupational/residential risk assessments. The study is also appropriate for acute dietary risk assessment for population subgroup females (13-50) because the aPAD for Acute Dietary exposure (0.017 mg/kg) for general population is protective of developmental effects (aPAD = 0.025 mg/kg). Decrease in body weight gain was the basis for the endpoints selected for chronic dietary and chronic dermal or inhalation occupational/residential risk assessments, although mild hepatotoxicity or neurological effects were seen at higher doses. The Uncertainty Factor(s) ranged from 100 to 300 depending on the type of exposure scenario (acute, short term, intermediate term or long term; oral, dermal, or inhalation) and the type of exposure assessment (occupational vs residential). HED selected doses and endpoints for risk assessment based solely on animal studies.

The Food Quality Protection Act (FQPA) Safety Factor Committee evaluated the hazard and exposure data and determined that the safety factor could be reduced to 3x for ziram because there is no quantitative or qualitative evidence of increased susceptibility following *in utero* exposure to rats and rabbits and/or following pre-/postnatal exposure to rats in the standard developmental and reproduction studies with ziram; and the dietary (food and drinking water) and residential exposure assessments will not underestimate the potential exposure for infants, children, and/or women of childbearing age. The Committee concluded that the safety factor is required for all population subgroups when assessing dietary and residential exposures of all durations since there is quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats.

Dietary exposure to ziram residues may occur as a result of use of ziram on fruits, and nut and vegetable crops. The peach washing study shows that ziram residues are found on the surface of the fruit and washing the fruit has been shown to greatly reduce ziram residues. With the exception of nuts all commodities for which ziram is registered are considered high consumption food items for infants and children. Insufficient data are available to ascertain the adequacy of the established tolerances for

blackberries, blueberries, grapes, and tomatoes (adequate for tolerance with regional registration only). The Residue data requirements for ziram have been partially fulfilled.

The enforcement methods (Pesticide Analytical Manual (PAM)) are based on the decomposition of dithiocarbamates including ziram with release of carbon disulfide (CS₂). However, the nature of the residues found in plants and animals is not completely known. The HED MARC has no objection to proceeding with the subject ziram RED and with risk assessments, given that the current CS₂ common moiety method would likely include the residues of toxicological concern. However, the analytical method cannot distinguish between ziram and ziram metabolites, nor can it distinguish between ziram and other dithiocarbamates including ferbam, thiram, or the ethylene-bis-dithio-scarbamates (EBDCs) which also degrade to CS₂. The toxicology studies were conducted using technical ziram. In the reregistration document, the dietary exposure assessment compares residues expressed as ziram, per se, to the toxicity endpoints expressed in terms of ziram, per se. However, the tolerances currently are expressed as zineb, but to harmonize with CODEX it is proposed that they should be expressed in terms of CS₂.

Uses supported by the Ziram Task Force include use as a fungicide on almonds, apples, apricots, blackberries, blueberries, cherries, grapes, nectarines, peaches, pears, pecans, tomatoes, ornamentals and as an industrial preservative in caulks, adhesives, sealant, wallboards and exterior latex paint. In addition, use on strawberries is also considered in the dietary exposure analyses (refer to use closure memorandum, May 22, 2001). The probabilistic dietary assessments employing use of the Dietary Exposure Evaluation Model (DEEM™) software reflect the use of field trial data and percent crop treated information and could be refined upon submission of monitoring data and studies for residue reduction such as washing and processing studies.

EFED has concluded that based on the available data, ziram is not persistent in the environment. The hydrolysis and photolysis half-lives are 0.74 and 0.36 days, respectively. The half-life in aerobic soil is 5.25 days. Ziram does not leach beyond 12 inches in the soil. In the environment, major volatile degradates of ziram are CO₂ and CS₂. The Environmental Fate and Effects Division (EFED) used Tier II screening models, PRZM/EXAMS, to evaluate the potential for ziram to contaminate water from its use. Monitoring data were not available for the drinking water risk assessment. The estimated environmental concentrations (EECs) of ziram in ground and surface water were derived using a conservative screening level models.

Residential handler exposure via dermal and inhalation routes can occur from use as a rabbit repellent on outdoor ornamentals such as trees, shrubs and flowers. Residential secondary handler exposure via dermal and inhalation routes may also occur during painting with ziram treated exterior grade latex paint. Exposure of residential secondary handlers from painting and from the rabbit repellent use are expected to be of a short-term duration (less than 30 days).

Occupational exposure to ziram can occur from agricultural, ornamental and antimicrobial uses. The exposure duration for short-term assessments is 1 to 30 days. Intermediate-term durations are greater than 30 days to six months. The toxicological endpoints selected for both short- and intermediate-term dermal and inhalation routes of exposure are the same and therefore, the risks are aggregated. No chronic (i.e., more than 180 days per year) antimicrobial, agricultural, ornamental, or residential uses have been identified.

In conclusion, the Agency finds that the estimated acute dietary (food) exposures exceed HED's level of concern for all infants, and children (1-6 years old) at the 99.9th percentile. However, after applying the reduction factor (0.15X) from the peach washing study to all commodities (except nuts and berries) the maximum dietary risk estimates are below HED's level of concern for all population subgroups. The data

indicates that washing can reduce residues by at least 85%. Additional washing study data are therefore, required as confirmatory data. When the required washing studies are submitted by the registrant, HED can better judge the reasonableness of the washing reduction factor.

The estimated chronic dietary risks are below HED's level of concern for all population subgroups. Based on the revised cancer classification of ziram ("Suggestive of carcinogenicity to humans") a quantitative assessment of human carcinogenic risk is not required.

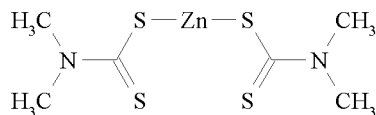
The EECs for surface water were greater than the acute DWLOCs, for three population subgroups (infants, children 1-6, and children 7-12 years), indicating that one-day maximum exposure to ziram in surface water plus one-day exposures to ziram in food (without applying reduction factor from washing study), at the 99.9th percentile of exposure exceeds HED's level of concern for these subgroups. After applying a reduction factor from the peach washing study, the EECs for surface water were greater than the acute DWLOCs for the 1-6 year child population subgroup only. The EECs for surface water (PRZM/EXAMS) and groundwater (SCI-GROW) were less than the chronic DWLOCs, indicating that chronic exposure to ziram in food and water is less than HED's level of concern. The aggregate chronic dietary (food + water) risk estimates do not exceed HED's level of concern.

The non-occupational dermal and inhalation exposures of residential handlers to ziram from Rabbit Scat do not exceed HED's level of concern. The postapplication exposures for both adults and children from residential use are expected to be minimal because of the nature of the residential application (foliar applications to outdoor ornamentals). Therefore, a post application risk assessment is not necessary at this time.

The short-term secondary dermal and inhalation exposures of residential painters from ziram-treated in-can preservative use (while using airless sprayers) alone are of concern. Based on the CARC's revised the cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required. An aggregate assessment for average daily dietary, short-term residential dermal and inhalation exposures of homeowners to Rabbit Scat or residential painters to paint from use of paint brush indicates that the chronic EECs are below the calculated short-term DWLOCs and therefore, aggregate risks from use of Rabbit Scat or use of paint brush are not of concern. Postapplication dermal and inhalation exposure in residential settings from the antimicrobial uses (e.g., exterior latex paint, caulks, adhesives) are expected to be negligible due to low vapor pressure of ziram and low dermal contact potential to treated surfaces. Therefore, dermal and inhalation exposure risks were not estimated.

Agricultural handler, antimicrobial primary handler short- and intermediate-term exposure estimates, do not exceed HED's level of concern with the proper mitigation measures detailed in the document. However, short- and intermediate-term secondary dermal and inhalation exposures to commercial painters from ziram in-can preservative use are of concern. Based on the CARC's revised the cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

2.0 Physical/Chemical Properties Characterization



Empirical Formula:	C ₆ H ₁₂ N ₂ S ₄ Zn	
Molecular Weight:		305.8
CAS Registry No.:		137-30-4
PC Code:		034805

Ziram [zinc dimethyldithiocarbamate] is a white powder with a melting point of 225.5-251 C, density of 1.7097 g/mL, vapor pressure of 1.8×10^{-5} Pa at 25 C (1.4×10^{-7} mmHg), and octanol/water partition coefficient ($\log P_{ow}$) of 1.65 at 20 C. Ziram is soluble in water at 65 ppm, slightly soluble in diethyl ether and ethanol, moderately soluble in acetone, and soluble in dilute alkali, carbon disulfide, and chloroform. Note that HED is requiring submission of additional studies on the solubility of Ziram. Ziram is incompatible with copper and mercury compounds, but is the most stable of the metallic dimethyldithiocarbamates.

A search of the Reference Files System (REFS) conducted 8/7/01 identified two registered manufacturing-use products (MPs) under PC Code 034805: the Elf Atochem North America Inc. 98% technical (T; EPA Reg. No. 4581-261) and UCB Chemicals Corporation 98% T (EPA Reg. No. 45728-14). In addition, R.T. Vanderbilt Company, Inc. produces one end-use product (96% EP; EPA Reg. Nos. 1965-79) by an integrated formulation system. Ziram is not persistent in the environment. The hydrolysis and photolysis half-lives are 0.74 and 0.36 days, respectively. The half-life in aerobic soil is 5.25 days. Ziram does not leach beyond 12 inches in the soil.

3.0 Hazard Characterization

3.1 Hazard Profile

The toxicology database for ziram is largely complete with respect to the OPPTS Guideline requirements with the exception of data gaps for morphometric analyses of brain tissues and statistical analyses of the neurobehavioral data gathered in the developmental neurotoxicity study, a dominant lethal study and a metabolite identification study in rats. The acute toxicity endpoints, utilized to establish the appropriate labeling parameters, are summarized in Table 1. The toxicological database indicates that ziram is a severe eye irritant (Toxicity Category I), exhibits moderate acute toxicity via the oral and inhalation routes and low toxicity via the dermal route (placed in Toxicity Categories II for the oral, inhalation routes and III for dermal route). It is not irritating to the skin (Toxicity category IV) and is a moderate dermal sensitizer.

Table 1. Acute toxicity of Ziram			
Guideline No./Study Type	MRIDs	Results	Tox Category
870.1100 Acute Oral	41340401 ^a	LD ₅₀ = 320 mg/kg (M&F) LD ₅₀ = 381 mg/kg (M) LD ₅₀ = 267 mg/kg (F)	II
	42429301 ^b	LD ₅₀ > 2000 mg/kg (M&F)	III
	43701301 ^a	LD ₅₀ = 2068 mg/kg (M&F) LD ₅₀ = 2719 mg/kg (M) LD ₅₀ = 2060 mg/kg (F)	III
870.1200 Acute Dermal	41340402 ^a	LD ₅₀ > 2000 mg/kg (M & F)	III
870.1300 Acute Inhalation	41442001 ^a	LC ₅₀ = 0.07 mg/L (M&F)	II
		LC ₅₀ = 0.08 mg/L (M)	
		LC ₅₀ = 0.06 mg/L (F)	
870.2400 Primary Eye Irritation	41643001 ^a	Severe irritation	I
	41454401 ^b	Severe irritation	I
870.2500 Primary Skin Irritation	41643002 ^a	Not a dermal irritant	IV
	41454602 ^b	Not a dermal irritant	IV
870.2600 Dermal Sensitization	41643003 ^a	Moderate dermal sensitizer; 30% sensitization rate	NA

a Technical b 76% formulation

The primary target organs of ziram appear to be the nervous system, liver and thyroid. A single oral dose causes neurological impairments while repeated short term exposure results in inhibition of brain cholinesterase and brain neurotoxic esterase in rats. Liver histopathology, sometimes accompanied by increases in hepatic serum enzyme levels, was seen at various doses in the subchronic and chronic rat studies and the mouse carcinogenicity study. Long-term dietary administration of ziram resulted in an increased incidence of thyroid C-cell hyperplasia, benign hemangiomas and thyroid C-cell tumors in male rats, and pulmonary alveolar/bronchiolar tumors in female mice. According to the Agency's *Draft Guidelines for Cancer Risk Assessment* (July, 1999), the CARC, on December 5, 2002, classified ziram into category "Suggestive of carcinogenicity to humans" based on the occurrence of hemangiomas and, possibly, preputial gland adenomas in male CD and F344 rats, respectively. The Committee further recommended that no quantification of human carcinogenic risk be determined for Ziram. In addition, the Committee determined that no conclusion can be reached regarding the potential of ziram to induce chromosome aberrations in the whole animal. Based on the acceptable *in vitro* data with purified ziram, an *in vivo* concern is not apparent. This is supported by the evidence showing positive results but only when the purity of ziram is <90% or not known. Since test material purity has become a major issue regarding mammalian cell genotoxicity and carcinogenicity, it should not be ignored for the *in vivo* genetic toxicology data. Based on these considerations, it is concluded that ziram consistently induces gene mutations in *Salmonella typhimurium*, however, this finding is not predictive of carcinogenesis since noncarcinogenic dimethyldithiocarbamates are also positive for gene mutations in *S. typhimurium*. The available studies submitted by the registrant satisfy the pre-1991 test guidelines for mutagenicity. There is no concern for mutagenicity at this time.

Table 2. Ziram Toxicology Profile

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-Day oral toxicity-rat	42450301 (1992) Acceptable/guideline 0, 100, 300, 1000 ppm M: 0, 7.4, 21.4, 67.8 mg/kg/day F: 0, 8.8, 24.2, 76.9 mg/kg/day	NOAEL = [M: 7.4, F: 8.8] mg/kg/day LOAEL = [M: 21.4, F: 24.2] mg/kg/day based on decreases in body weight, body weight gain, food consumption, and minimal histopathological changes in the female liver
870.3150 90-Day oral toxicity-dog	N/A (requirement fulfilled by chronic dog study)	N/A
870.3200 21/28-Day dermal toxicity-rabbit	41297001 (1989) Acceptable/guideline M&F: 0, 100, 300, 1000 mg/kg	NOAEL = [M: >1000, F: 300] mg/kg LOAEL = [F: 1000] mg/kg based on decreased body weight and food consumption and clinical chemistry suggestive of minimal hepatotoxicity. A LOAEL was not observed in males.
870.3250 90-Day dermal toxicity	NA	NA
870.3465 90-Day inhalation toxicity	NA	NA
870.3700a Prenatal developmental-rat	41908701 (1990) Acceptable/guideline F: 0, 1, 4, 16, 64 mg/kg/day	Maternal NOAEL = [4] mg/kg/day LOAEL = [16] mg/kg/day based on decreased body weights, reduced food consumption, salivation, and increased water intake. Developmental NOAEL = [4] mg/kg/day LOAEL = [16] mg/kg/day based diaphragmatic thinning
870.3700b Prenatal developmental-rabbit	00161316 (1986) Acceptable/guideline F: 0, 3, 7.5, 15 mg/kg/day	Maternal NOAEL = [3] mg/kg/day LOAEL = [7.5] mg/kg/day based on decreased body weight gain. Developmental NOAEL = [7.5] mg/kg/day LOAEL = [15] mg/kg/day based on increased incidence of resorptions and post-implantation loss.
870.3800 Reproduction and fertility effects-rat	43935801 (1996) Acceptable/guideline 0, 72, 207, 540 ppm F ₀ males: 0, 5.3, 14.8, 37.5 mg/kg/day F ₀ females: 0, 6.1, 16.8, 42.8 mg/kg/day F ₁ males: 0, 5.6, 16.7, 42.7 mg/kg/day F ₁ females: 0, 6.3, 18.4, 47.5 mg/kg/day	Parental/Systemic NOAEL = [14.8] mg/kg/day LOAEL = [37.5] mg/kg/day based on reduced body weights, body weights gains, and food consumption in the F ₀ and F ₁ males and females. Offspring NOAEL = [16.8] mg/kg/day LOAEL = [42.8] mg/kg/day based on decreased body weights at birth in F ₂ pups and during lactation in F ₁ and F ₂ pups.

Table 2. Ziram Toxicology Profile

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4100a Chronic toxicity-CD rat	43404201 (1994) Acceptable/guideline 0, 60, 180, 540 ppm M: 0, 2.5, 7.7, 23.7 mg/kg/day F: 0, 3.4, 10.2, 34.6 mg/kg/day	NOAEL = not established LOAEL = [M: 2.5, F: 3.4] mg/kg/day based on histopathological findings in various organs.
870.4100a Chronic toxicity- F344 rat	NTP (1983) Acceptable/guideline 0, 300, or 600 ppm M: 0, 11, or 22 mg/kg/day F: 0, 13, or 26 mg/kg/day	NOAEL = [M: 22, F: 26] mg/kg/day based on lack of effect. LOAEL = [M: >22, F: >26] mg/kg/day
870.4100a Chronic toxicity- F344 rat	45770201 (1983) Acceptable/guideline 0, 20, 200, or 2,000 ppm M: 0, 0.70, 6.9, or 74 mg/kg/day F: 0, 0.83, 8.5, or 91 mg/kg/day	NOAEL = [M: 0.70, F: 0.83] mg/kg/day LOAEL = [M: 6.9, F: 8.5] mg/kg/day based on slight anemia in females, decreases in the absolute and relative weight of the crural muscle in both sexes, atrophy of the crural muscle in both sexes, increased mucosal cornification of the stomach in both sexes, follicular cell hypertrophy of the thyroid in females, and rhinitis of the nasal cavity in females.
870.4100b Chronic toxicity- dog	42823901 (1993) Acceptable/guideline 0, 50, 185, 700 ppm M: 0, 1.6, 6.6, 17.4 mg/kg/day F: 0, 1.9, 6.7, 20.6 mg/kg/day	NOAEL = [M: 1.6, F: 1.9] mg/kg/day LOAEL = [M: 6.6, F: 6.7] mg/kg/day based on decrease in body weight gain in the females and liver histopathology in males.
870.4200a Carcinogenicity- CD rat	Same as chronic toxicity-CD rat above (870.4100a).	Evidence of carcinogenicity based on increased incidence of benign hemangiomas in CD male rats at 23.7 mg/kg/day
870.4200a Carcinogenicity- F344 rat	Same as chronic toxicity-F344 rat above (870.4100a).	Evidence of carcinogenicity based on increased incidence of thyroid C-cell carcinoma in male rats at 22 mg/kg/day
870.4200a Carcinogenicity- F344 rat	Same as chronic toxicity-F344 rat above (870.4100a).	Evidence of carcinogenicity based on increased incidence of preputial gland adenomas in male rats at 74 mg/kg/day.
870.4200b Chronic/Carcinogenicity- CD-1 mouse	43373701 (1994) Acceptable/guideline 0, 29, 75, 225, 675 ppm M: 0, 3, 9, 27, 82 mg/kg/day F: 0, 4, 11, 33, 95 mg/kg/day	NOAEL = [M: 9, F: 11] mg/kg/day LOAEL = [M: 27, F: 33] mg/kg/day based on decreased absolute brain weight in both sexes and increased incidence of urinary bladder epithelial hyperplasia and decreased body weight gain in CD-1 males. No evidence of carcinogenicity

Table 2. Ziram Toxicology Profile

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4200b Chronic/Carcinogenicity- B6C3F1 mouse	NTP (1983) Acceptable/guideline 0, 600, or 1200 ppm M: 0, 122, or 196 mg/kg/day F: 0, 131, or 248 mg/kg/day	NOAEL = [M:196]mg/kg/day; not established for females; LOAEL = [M: >196, F: 131] mg/kg/day based on increased incidence of alveolar epithelial hyperplasia in females Evidence of carcinogenicity based on increased incidence of alveolar/bronchiolar adenomas and of combined alveolar/bronchiolar adenomas or carcinomas in female B6C3F1 mice at ≥ 131 mg/kg./day
Gene Mutation 870.5265 Salmonella/ mammalian activation gene mutation assay	00147462 (1984) Acceptable/guideline 41642901 (1990) Acceptable/guideline Haworth, et al. (1983) Acceptable/guideline	The test article was positive for gene mutation induction in strain TA100 (\pm S9). The test article was mutagenic when tested above 50 μ g/plate (+S9). The test article was positive in strains TA100 (\pm S9) and TA1535 (+S9)
Cytogenetics 870.5375 <i>in vitro</i> mammalian cytogenetics assay	41287802 (1989) Acceptable/guideline Gulati (1989) Acceptable/guideline	There was no evidence of structural chromosomal aberrations over background. The test article was positive for chromosomal aberrations (\pm S9).
870.5300 mammalian cell gene mutation assay	45806501(1999) Acceptable/guideline	No reproducible increase in the mutation frequency of mouse lymphoma cells was seen
870.5300 mammalian cell gene mutation assay	McGregor, et al. (1988) Acceptable/guideline	The test article was positive for gene mutation induction (-S9).
870.5395 mammalian erythrocyte micronucleus test	Proudock, R.L. and Taylor, K. (1992) Unacceptable - maximum tolerated dose not tested, dosing regime not justified, and non-standard procedures used.	The test article was negative in the peripheral blood of CD-1 Swiss mice fed levels of 25, 75, 225, or 675 ppm for 89 days.
Other Genotoxicity 870.5550, Unscheduled DNA synthesis	41287801 (1989) Acceptable/guideline	There was no evidence that unscheduled DNA synthesis was induced.
870.6200a Acute neurotoxicity screening battery	43362801 (1994) Acceptable/guideline M&F: 0, 15, 300, 600 mg/kg	NOAEL = not established LOAEL = [M&F: 15] mg/kg/day based on ataxia and slight impairment of gait in males.

Table 2. Ziram Toxicology Profile		
Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.6200b Subchronic neurotoxicity screening battery	43413701 (1994) Acceptable/guideline 0, 72, 207, 540 ppm M: 0, 5, 14, 34 mg/kg/day F: 0, 6, 16, 40 mg/kg/day	Systemic NOAEL = [M: 14, F: 16] mg/kg/day LOAEL = [M: 34, F: 40] mg/kg/day based on decreased body weight and body weight gains. Cholinesterase NOAEL = [M: 14, F: 6] mg/kg/day LOAEL = [M: 34, F: 16] mg/kg/day based on brain cholinesterase inhibition in both sexes and brain neurotoxic esterase activity in the males.
870.6300 Developmental neurotoxicity	43935801 (1996) Unacceptable/guideline 0, 72, 207, 540 ppm Maternal gestation: 0, 5, 13, 32 mg/kg/day Maternal lactation: 0, 11, 30, 79 mg/kg/day	Maternal NOAEL = [13] mg/kg/day LOAEL = [32] mg/kg/day based on reduced body weights and/or body weights gains, and decreased food consumption during gestation and lactation. Offspring NOAEL = not established LOAEL = [5] mg/kg/day based on increased motor activity.
870.7485 Metabolism and pharmacokinetics-rat	42391001 (1992) Unacceptable/guideline M&F: 15, 352 mg/kg or 15 mg/kg/day	The test material was rapidly absorbed and excreted via the urine and expired air, and significant amounts were excreted in the feces. Small amounts were widely distributed in the body. Metabolites were not identified.
870.7600 Dermal penetration	Same as 21-day dermal rabbit (870.3200) and rabbit oral developmental (870.7600).	The test material was minimally absorbed.

3.2 FQPA Considerations

The FQPA SFC recommended that the FQPA safety factor is necessary for protection of infants and children (as required by FQPA) when assessing the risk posed by ziram since:

- ▶ there is quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats; and
- ▶ there are data gaps in the developmental neurotoxicity study with ziram (morphometric analysis);

However the safety factor could be **reduced to 3x** for ziram because:

- ▶ There is no quantitative or qualitative evidence of increased susceptibility following *in utero* exposure to rats and rabbits and following pre-/postnatal exposure to rats in the standard developmental and reproduction studies with ziram;
- ▶ With respect to the data gaps identified in the toxicity data base for ziram, the outstanding data from the DNT (morphometric analysis) may confirm and characterize the effects seen with ziram - but not increase the concern for the effects; and
- ▶ The dietary (food and drinking water) and residential exposure assessments will not underestimate the potential exposure for infants, children, and/or women of childbearing age.

The safety factor is required for **All Population Subgroups** when assessing **Dietary and Residential Exposures of All Durations** since there is quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats.

3.3 Dose Response Assessment

On September 6, 2001, the Health Effects Division (HED) Hazard Identification Assessment Review Committee reevaluated the toxicology data base of ziram, established acute and chronic reference doses (RfD's) for dietary exposure and selected the toxicological endpoints for occupational exposure and residential risk assessments. There is high degree of confidence in the quality of data and in the hazard and dose response assessments. Table 3 summarizes the doses and endpoints selected for use in this human health risk assessment.

Table 3. Summary of endpoints			
EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (Female 13+) ^{1,2}	NOAEL = 7.5 UF=100 FQPA SF=3	Increased incidence of resorptions and post implantation loss	Prenatal Oral Developmental / Rabbit
		Acute RfD (Female 13-50) = 0.075 mg/kg Acute Population Adjusted Dose (aPAD) = 0.025 mg/kg/day	
Acute Dietary (Gen. Population) ^{1,2}	LOAEL = 15 UF = 300 FQPA SF = 3	Ataxia and slight impairment of gait	Acute Oral Neurotoxicity / Rat
		Acute RfD (Gen. Population) = 0.05 mg/kg Acute Population Adjusted Dose (aPAD) = 0.017 mg/kg/day	
Chronic Dietary	NOAEL = 1.6 UF = 100 FQPA SF = 3	Decreased body weight gain at a LOAEL of 6.6 mg/kg/day	52-Week Oral Toxicity / Dog
		Chronic RfD = 0.016 mg/kg/day Chronic Population Adjusted Dose (cPAD) = 0.005 mg/kg/day	
Dermal, Short- and Intermediate-Term ^{3,4}	NOAEL = 7.5 MOE = 100 (Occupational) ⁵ and 300 (Residential)	Increased incidence of resorptions and post implantation loss	Prenatal Oral Developmental / Rabbit
Dermal, Long-Term	NOAEL = 1.6 MOE = 100 (Occupational) and 300 (Residential)	Decreased body weight gain.	52-Week Oral Toxicity / Dog
Inhalation, Short- and Intermediate-Term	NOAEL = 7.5 MOE = 100 (Occupational) ⁵ and 300 (Residential)	Increased incidence of resorptions and post implantation loss	Prenatal Oral Developmental / Rabbit
Inhalation, Long-Term	NOAEL = 1.6 MOE = 100 (Occupational) and 300 (Residential)	Decreased body weight gain.	52-Week Oral Toxicity / Dog

1. The dose and endpoint for population subgroup Females (13-50) was not selected for risk assessment because the aPAD for Acute Dietary exposure (0.017 mg/kg) for general population is protective of developmental effects which are selected as an endpoint for Females (13-50) (aPAD (0.025 mg/kg).

2. FQPA SF of 3x for all dietary and residential exposure/risk assessments was applied.

3. The appropriate dermal (1%) or inhalation absorption factor (100%) was used since the NOAEL is from an oral study.

4. Residential MOE (Margin of Exposure) = 100xSF 3x=300; occupational MOE for all durations=100

5. The dermal and inhalation MOEs for the occupational exposure of short-term duration are combined because the toxicological effects are the same (increased incidence of resorptions and post implantation loss). The dermal and inhalation MOEs for the occupational exposure of intermediate-term duration are combined because the toxicological effects are the same (increased incidence of resorptions and post implantation loss).

3.4 Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruption Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, ziram may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 Exposure Assessment and Characterization

4.1 Summary of Registered Uses

Ziram is registered for use on variety of stone fruits, pome fruits, nut and vegetable crops including almonds, apples, apricots, blackberries, cherries, grapes, nectarines, peaches, pears, pecans, and tomatoes. In addition use on strawberries (refer to use closure memo) is also considered in the dietary assessment. Applications of ziram include dormant, pre-bloom, preharvest and foliar treatments. The nonfood uses of ziram include ornamental plants (i.e. flowering plants, nursery plants, pine seedlings, Douglas and Shasta firs). Ziram is also used as a preservative in adhesives, caulks, sealants, wallboard, and exterior latex paint. Ziram is registered for direct residential applications on outdoor ornamentals (trees, shrubs and flowers) as a repellent product, Rabbit Scat.

Ziram is available as dry flowable (DF), wettable powder, and liquid formulations. Ziram may be applied with groundboom and aerial equipment or airblast sprayer. For other specialty uses (i.e. rabbit repellent), applications may be made using hand held equipment.

4.2 Dietary Exposure/Risk Pathway

4.2.1 Residue Profile

Tolerances have been established for residues of ziram (40 CFR §180.116), calculated as zinc ethylenedisithiocarbamate (zineb). These tolerances are established at 7 ppm except those established for almonds and pecans which are set at 0.1 ppm each. No tolerances have been established for ziram residues in livestock or processed food/feed commodities. Most of the ziram tolerances were set during the 1950 Spray Residue Hearings. Insufficient data are available to ascertain the adequacy of the established tolerances for blackberries, grapes, and tomatoes or the need for tolerances in livestock commodities. The residue chemistry data requirements for ziram have been partially fulfilled.

Dietary exposure to Ziram residues may occur as a result of use of ziram on fruits, and nut and vegetable crops. With the exception of nuts all commodities for which ziram is registered are considered high consumption food items for infants and children. Although the nature of the residue in plants and animals is not adequately understood, the HED MARC has no objection to proceeding with the subject ziram RED and with risk assessments, given that the current common moiety method would likely include the residues

of toxicological concern.

The enforcement methods (Pesticide Analytical Manual (PAM)) are based on the decomposition of dithiocarbamates with release of carbon disulfide (CS_2). The ziram residues of concern are expected to contain the CS_2 moiety, and can be determined by the analytical method. However, the analytical method cannot distinguish between ziram and ziram metabolites, nor can it distinguish between ziram and other thiocarbamates including ferbam, thiram, or the ethylenebisdithiocarbamates or EBDCs which degrade to CS_2 . The residue data are expressed in terms of ziram, per se. However, the tolerances currently are expressed in the form of zineb, but to harmonize with CODEX it is proposed that they should be expressed in terms of CS_2 .

The acute dietary probabilistic assessments conducted using the Dietary Exposure Evaluation Model (DEEM™) reflect the use of anticipated residues based on field trial data and percent crop treated information, the hazard endpoint and dose derived from an Acute Oral Neurotoxicity Study in Rats, and the FQPA Factor. No field trial data were available for strawberry, and blackberry, therefore, tolerances were used in the dietary exposure analyses for these commodities. Ziram residues are found on the surface of the fruit and are not systemic in plants. Therefore, use of a reduction factor due to washing is a viable way to refine the risk estimates. In calculating dietary risk, a reduction factor from the peach washing study was applied. It could be refined upon submission of additional washing and processing studies. Dietary risks have been presented with and without the washing reduction factor for comparative purposes.

FDA monitoring data from 1992-1999 were available for the dithiocarbamate class of pesticides for the following commodities: apples, pears, peaches, nectarines, tomatoes, and several of the small berries. The common moiety analytical method would determine ziram residues along with a number of other pesticides. However, all commodities had less than 100 samples which were monitored for ziram except for tomato. It is the policy of HED not to use monitoring data with less than 100 samples. Since tomatoes were not a risk driver in the dietary analyses the tomato FDA data were not used either.

Residues of ziram in/on fruit, nut and vegetable crops derived from field trials were considered in this risk assessment. Chronic dietary risks were calculated using the dose and endpoints selected from a Chronic Oral Toxicity Study in Dogs, DEEM™ Software, average field trial data, percent crop treated data, and the FQPA factor. In both assessments, dietary exposure (consumption) was compared to a population adjusted dose (PAD), which is the reference dose (RfD) reflecting application of the FQPA 3x safety factor. The acute PAD is 0.025 mg/kg/day for female 13+ and 0.017 mg/kg/day, for remaining subpopulations. The chronic PAD is 0.005 mg/kg/day for all subpopulations. HED considers dietary residue contributions greater than 100% of the PAD to be of concern. Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

Refer to Product and Residue Chemistry Chapter (01/17/02, D280352) and Anticipated Residues, Acute, Chronic, and Cancer Dietary Exposure and Risk Analyses (01/16/2002, D280195) for further details.

Note: the quantitative cancer assessment provided in the Dietary Exposure and Risk Assessment document is no longer applicable because the cancer classification has been revised.

4.2.2 Acute Dietary

Acute dietary exposure analyses for ziram are reported as a percentage of the acute Population Adjusted Dose (aPAD) for the 99.9th percentile of the population. The estimated acute dietary exposure exceeds HED's level of concern for All Infants and Children (1-6 years old) at the 99.9th percentile. Without using the 0.15x reduction factor, the subpopulation with highest risk was All Infants with estimated exposure of 175% of the aPAD followed by Children (1-6 years old) at 125% of the aPAD.. For the U.S. population the estimated exposure was at 68% of the aPAD (Table # 5).

When the 0.15x reduction factor from the peach washing study was applied to all commodities (except nuts and berries) the maximum dietary risk estimates were below the HED's level of concern of 100% for all population subgroups (Table # 4).

Table 4. Estimated Acute Dietary Exposure and Risk for Ziram using field trials and applying the 0.15x reduction factor from the peach washing study to all commodities except nuts and berries.

Population Subgroup	Acute (99.9th %-ile)	
	Exposure (mg/kg/day)	%aPAD
U.S. Population	0.0025	14
All infants (<1 yr)	0.0045	26
Children (1-6 yrs)	0.0100	57
Children (7-12 yrs)	0.0036	21
Females (13-50 yrs)	0.0017	10
Males (13-19 yrs)	0.0012	7
Males (20+ yrs)	0.0016	9
Seniors (55+ yrs)	0.0018	10

4.2.3 Chronic Dietary

Chronic dietary exposure to ziram which was calculated using average residues, average consumption, and percent crop treated data was compared to the cPAD. Without using the 0.15 x reduction factor, the estimated chronic dietary risks are below HED's level of concern for all population subgroups. The resulting risk estimates did not exceed 26% of the cPAD for any subpopulation which is below the Agency's level of concern of 100% (Table #5).

Table 5. Estimated Acute and Chronic Dietary Exposure and Risk for Ziram using field trials without reduction factor

Population Subgroup	Acute (99.9th %-ile)		Chronic	
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% cPAD
U.S. Population	0.0112	66	0.0003	6
All infants (<1 yr)	0.0300	175	0.0014	26
Children (1-6 yrs)	0.0212	125	0.0009	18
Children (7-12 yrs)	0.0123	72	0.0006	11
Females (13-50 yrs)	0.0060	35	0.0002	4
Males (13-19 yrs)	0.0048	28	0.0002	3
Males (20+ yrs)	0.0057	34	0.0002	4
Seniors (55+ yrs)	0.0072	42	0.0003	5

4.2.4 Cancer Dietary

Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

4.3 Water Exposure/Risk Pathway

The Environmental Fate and Effects Division (EFED) has concluded that based on the available data, ziram is not persistent in the environment. The hydrolysis and photolysis half-life is 0.74 and 0.36 days, respectively. The half-life in aerobic soil is 5.25 days. In the environment, the major volatile degradates of ziram are CO₂ and CS₂. Monitoring data were not available for the drinking water risk assessment. The estimated environmental concentrations (EECs) of ziram found in ground and surface water were derived using conservative screening level model, PRZM/EXAMS. Upon hydrolysis and soil photolysis, ziram quickly degrades to thiram. However, the data are not sufficient to quantify the amount of thiram formed from ziram..

HED uses Drinking Water Levels of Comparison (DWLOCs) values as a surrogate measure of exposure. A DWLOC or drinking water level of concern is theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. The models currently used to estimate pesticide concentrations in drinking water are very conservative and used as screening tools in the risk assessment process. The current model estimates from GENEEC, PRZM/EXAMS and SCI-GROW are compared to DWLOC values. This comparison provides a semi- quantitative risk assessment for drinking water until monitoring data can be obtained. The Environmental Fate and Effects Division (EFED) used the Tier II PRZM/EXAMS screening model to evaluate the potential for ziram to contaminate water from its use.

As shown below, for ziram, the peak surface water concentrations estimated are 98 ppb, and the chronic (annual average) concentrations are 1.98 ppb. For groundwater, the estimated peak and annual average concentration is 0.03 ppb. Residues in water are based on the maximum labeled application rate.

Tier II PRZM/EXAM and SCI-GROW Estimated Environmental Concentrations (EECs) for ziram use on apples, pears, and peaches (Western U.S.)

Model	EECs (ug/L)
Surface Water (PRZM/EXAM)	Peak = 98 ppb Annual Average = 1.98 ppb
Groundwater (SCI-GROW)	0.03 ppb

Ziram does not seem to significantly leach into groundwater, due to its high soil/water partitioning coefficient. The field studies confirm the low leaching potential of this chemical in the field, as ziram was not detected in any of the soil samples below the 12" layer. Further discussion is found in the Tier II Surface Drinking Water Assessment.chapter (1/24/02, D280450).

4.4 Residential Exposure/Risk Pathway

The residential use is limited to outdoor foliar applications to ornamentals as a rabbit repellent along with an in-can paint preservative. Ziram is registered for direct residential applications as a rabbit repellent on outdoor-grown ornamentals. This can result in short-term dermal and inhalation exposure to home owners applying the product. In addition, residential secondary handler exposures can occur from ziram use as an in-can preservative in exterior grade latex paints. The secondary handlers are defined by EPA as those individuals exposed to the active ingredient as a direct result of its incorporation into an end use product (e.g., individuals using the caulk or paint that in itself is not a registered product). The Agency has estimated residential handler exposure and risks using data from the Pesticide Handlers Exposure Database (PHED, version 1.1), a surrogate carbaryl duster study, as well as the toxicological endpoints (increased incidence of resorptions and postimplantation loss in rabbit developmental study) chosen by the HIARC. The FQPA uncertainty factor of 3 x was applied to short-term residential risk assessments. [The carbaryl study is currently under consideration by the Outdoor Residential Exposure Task Force (ORETF), if purchased it will become part of the proprietary data base].

Residential postapplication exposures to the rabbit repellent are expected to be minimal because the product is only applied to outdoor-grown ornamentals. Unlike lawns, the ornamentals are expected to have a low potential for dermal contact from adults and children. Secondary postapplication exposures to ziram-containing paint are also expected to be minimal based on the low vapor pressure of ziram ($1.4\text{E-}7$ mmHg at 25 C) and the low potential contact with treated surfaces such as exterior painted surfaces, adhesives, and caulks.

4.4.1 Home Uses

Rabbit Scat, a ziram-containing rabbit repellent, is registered for direct residential application to ornamentals such as trees, shrubs and flowers. Short-term residential dermal and inhalation exposure of homeowners (secondary handlers) may also occur when painting with previously treated exterior grade latex paint containing ziram as an in-can preservative. The paint itself is not a registered pesticidal product. Postapplication exposures are expected to be minimal for both the rabbit repellent use and the exterior grade latex paint.

4.4.1.1 Residential Handler's Exposure from Rabbit Scat

The calculated combined MOEs for short term dermal and inhalation exposure/risk for home owners (combined mixer/loader/applicator) using **Rabbit Scat** are greater than or equal to 1400 (Table # 6). These MOES are greater than the target MOE of 300 for both scenarios and are below HED's level of

concern.

Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

4.4.1.2 Residential Secondary Handler's Exposure (applicator) from Antimicrobial Uses (e.g. Paint)

Residential applications of the exterior grade latex paint include painting with an airless sprayer and paint brushes (paint roller exposure data are not available but the magnitude of exposure is believed to be similar to that monitored for use of a paint brush). Although there is potential exposure during the application of the other treated materials (e.g., caulks and sealants), they are not included because no data are available to assess the uses. It is HED's professional judgement that the painting scenarios represent the high end exposures for ziram antimicrobial secondary uses. For the discussion of uncertainties refer to the HED's Occupational and Residential Exposure assessment document (D276788).

The secondary handlers are defined by EPA as those individuals exposed to the active ingredient as a direct result of its incorporation into an end use product. For secondary handlers, the residential short-term dermal and inhalation exposures to individuals exposed while using an airless sprayer is of concern; however, similar exposure to paint brush is not of concern. The combined dermal and inhalation MOEs are 74 for the airless sprayer and 350 for the paint brush (Table # 6). No mitigation measures, such as the use of chemical resistant gloves, are available for the secondary exposures because the individuals that are being exposed to paint containing ziram are exposed to products with no pesticide labels (i.e., in-can preservative use). The MOE of 74 for the airless sprayer is below the target MOE (Target MOE = 300). Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

4.4.1.3 Postapplication

For direct ziram applications, the postapplication exposures for both adults and children are expected to be minimal because ziram is only applied to outdoor ornamentals. Therefore, a post application risk assessment is not necessary at this time. Dermal and inhalation exposure in residential settings from the antimicrobial uses (e.g., exterior latex paint, caulks, adhesives) are expected to be negligible due to low vapor pressure of ziram and low dermal contact potential to treated surfaces.

4.4.1.4 Other (Spray Drift etc.)

HED also has concerns for the potential for children's exposure in the home as a result of agricultural uses of ziram. Potential environmental concentrations of ziram in homes may result from spray drift, track-in, or from redistribution of residues brought home on the farm worker's clothing. The Agency is currently in the process of revising its guidance for completing these types of assessments. Modifications to this assessment shall be incorporated as updated guidance becomes available. For further details refer to ziram's Occupational and Residential Exposure Assessment document (9/12/01; D276788).

Table 6. Short-Term Residential Use of Ziram.

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (µg/lb ai)	Crop	Application Rate	Amount Treated	Absorbed Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Mixer/Loader/Applicator										

Loading/Applied as a Dust	140	1200	Ornamentals	0.14 lb ai	1 container	0.0028	2700	0.0024	3100	1400
Low Pressure Handwand application	100	30	Ornamentals	0.0345 lb ai per gallon	2.5 Gallons	0.0012	6300	0.000037	200,000	6100

a,b

Dermal and inhalation unit exposures represent short pants and short sleeved shirts.

c

Application rates are based on the ziram label (RABBIT SCAT EPA Reg. No. 3772-24).

d

Amount treated is based on the entire 10 ounce contents for the dust and a 2.5 gallon sprayer for the dilute spray.

e

Absorbed dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai or lb ai/gallon) / Body weight (70 kg)].

f

MOE = NOAEL (mg/kg/day) / Daily Dose [Where short-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. The target MOE is 300.

g

Inhalation dose (mg/kg/day) = [unit exposure (µg/lb ai) * 0.001 mg/µg unit conversion * max appl rate (lb ai/A or lb ai/gal) * area treated (acres or gal) * 100 percent inhalation absorption] / Body weight (70 kg).

h

Total MOE = 1/[1/(dermal MOE) + (1/inhalation MOE)].

Table 7. Short- and Intermediate-term In-Can-Preservative Use of Ziram and MOEs.											
Exposure Scenario	Population Targeted	Clothing Attire	Dermal Unit Exposure (mg/lb ai) ^a	Inhalation Unit Exposure (µg/lb ai) ^b	Appl. Rate (lb ai/gal) ^c	Amount Treated	Absorbed Dermal Dose (mg/kg/d) ^e	Dermal MOE	Inhalation Dose (mg/kg/d) ^g	Inhalation MOE	Total MOE
Secondary Handlers: Short-term Residential Exposure Duration											
Airless Sprayers	Residential	Short pants, short sleeved shirt	79	830	0.29 max rate	15 gallons	0.049	150	0.052	150	74
Paint Brush	Residential	Short pants, short sleeved shirt	230	280	0.29 max rate	2 gallons	0.019	390	0.0023	3200	350

a,b

Dermal and inhalation unit exposures are from CMA study and PHED V1.1.

c

Application rates are from the ziram label (Vancide MZ-96 EPA Reg. No. 1965-79) along with density and % solid information from Vanderbilt Co.

d

Amount treated is based on assumptions from EPA's Antimicrobial Division and HED's Residential SOPs.

e

Abs. dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai/gallon) * gallons handled / Body weight (70 kg)].

f

MOE = NOAEL (mg/kg/day) / Daily Dose [Where short-and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. Target MOE is 100 for commercial and 300 for residential.

g

Inhalation dose (mg/kg/day) = [unit exposure (µg/lb ai) * 0.001 mg/µg unit conversion * max appl rate (lb ai/gal) * gallons handled * 1 inhalation absorption] / Body weight (70 kg).

h

Total MOE (short-term duration) = 1/[1/(dermal MOE) + (1/inhalation MOE)].

4.5 Incidents Reports

HED has reviewed the OPP Incident Data System (IDS), the Poison Control Center (PCC), the California Department of Food and Agriculture (Department of Pesticide Regulation), and the National Pesticide Telecommunications Network (NPTN) databases for reported incident information for ziram.

According to California and PCC data, it appears that a majority of cases involved skin and eye illnesses (e.g., skin rashes, conjunctivitis, and red, irritated, and itchy eyes and skin). Of the 23 Poison Center cases, 6 were non-occupational including one child under six years of age. A large proportion of cases resulted after field workers were exposed to ziram due to failure to wear, or use properly, their personal protective equipment. Appropriate personal protective equipment such as the use of skin and eye protection would protect workers who may have extensive exposure to ziram. Only one "other non-occupational" activity category incident was reported by California from 1982 to 1999.

For details refer to the Review of Incidents Reports (08/10/01, D276936).

5.0 Aggregate Risk Assessments and Risk Characterizations

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require that for establishing a pesticide tolerance "that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information." Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food, and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Aggregate risk assessments are typically conducted for acute (1 day), short-term (1-30 days), intermediate-term (30 days to several months), chronic (several months to lifetime) exposure.

The Agency considered aggregate exposure and risk estimates for residents who might be exposed to ziram from multiple sources, such as residential use, food, and water. Residential exposure and risk from the use of ziram was limited to short-term exposure scenarios (dermal and inhalation) because intermediate-term and chronic residential exposure to ziram is not expected to occur. The aggregate acute exposure to ziram in food (with or without reduction factor) and water exceeds HED's level of concern

5.1 Acute Risk

5.1.1 Aggregate Acute Risk Assessment

Using the DWLOC approach, aggregate acute risk considers total dietary risk from one day's consumption of food and water.

The Tier II EECs for surface water were greater than the acute DWLOCs, for all population subgroups indicating that one-day maximum exposure to ziram in surface water plus one-day exposures to ziram in food at the 99.9th percentile of exposure exceeds HED's level of concern (Table 8a). For All Infants and Children (1-6 years) the acute dietary exposure in food alone exceeds the level of concern. Effectively, the acute DWLOC for All Infants and Children (1-6 years) subpopulations is zero.

After applying the 0.15x reduction factor, the EECs for surface water were still higher than the acute DWLOCs, for all population subgroups indicating that one-day maximum exposure to ziram in surface water plus one-day exposures to ziram in food at the 99.9th percentile of exposure exceeds HED's level of concern (Table 8b).

5.1.2 Acute DWLOC Calculations

Currently, the model estimates of EECs are compared to a human health drinking water level of concern (DWLOC), which is the theoretical concentration of a pesticide in drinking water that would be an acceptable upper limit in light of the aggregate exposure to that pesticide from other sources (food and residential use). As the models are highly conservative, if the model estimate does not exceed the DWLOC, it can be concluded with reasonable certainty that the contribution from pesticide residues in drinking water does not exceed the Agency's level of concern. If an estimated acute dietary risks for a pesticide from the food contribution exceed HED's level of concern, then there is no allowable contribution for water to the risk cup.

For acute drinking water exposure, the DWLOC_{acute} was calculated based on the acute dietary (food) exposure and default body weights and water consumption. There was no acute oral residential exposure. The calculated Acute DWLOCs are found below in Table #8a. The calculations were also done using the 0.15x

washing factor for dietary exposure. These calculations are found in Table 8b. The EECs for groundwater (SCI-GROW) are less than DWLOCs for all population subgroups, indicating that acute exposure to ziram in food (with or without reduction factor) and groundwater is below HED's level of concern (Table #s 8a and b). The EECs for surface water (PRZM/EXAM) exceed DWLOCs calculated without the washing reduction factor for three population subgroups (infants, children 1-6, and children 7-12 years). For all other population subgroups, surface water EECs are below DWLOCs (without washing) and therefore below HED's level of concern. With the reduction factor included in the DWLOC calculation, surface water EECs exceed DWLOCs for the child 1-6 year subpopulation only. Surface water EECs are below DWLOCs (with washing) and therefore below HED's level of concern for all other population subgroups. The Agency's default body weights and water consumption used to calculate DWLOCs are as follows: 70 kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (infant). To calculate the acute DWLOC, the acute dietary food exposure was subtracted from the aPAD as shown in the following equation:

$$\text{DWLOC}_{\text{acute}} = \frac{[\text{one-day water exposure (mg/kg/day)} \times (\text{body weight})]}{[\text{consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$$

Where One-day Water Exposure (mg/kg/day) = $\text{Acute PAD (mg/kg/day)} - [\text{One-day Food Exposure exposure (mg/kg/day)}]$

Table 8a . Drinking Water Levels of Comparison for Acute Dietary Exposure without Reduction Factor						
Population Subgroup	Acute PAD (mg/kg/day)	Food Exposure at 99.9th percentile* (mg/kg/day)	Max. Water Exposure (mg/kg/day)	DWLOC _{acute} (ug/L)	Surface Water (ug/L) max.	Ground Water (ug/L)
US Population	0.017	0.0116	0.0058	203	98	0.03
All Infants	0.017	0.0300	Exceeds	zero	98	0.03
Children 1-6	0.017	0.0216	Exceeds	zero	98	0.03
Children 7-12	0.017	0.0123	0.0047	47	98	0.03
Females 13-50	0.017	0.0062	0.0110	329	98	0.03
Males 13-19	0.017	0.0049	0.0122	428	98	0.03
Males 20+	0.017	0.0066	0.0113	395	98	0.03
Seniors 55+	0.017	0.0072	0.0098	344	98	0.03

(a) 99.9th percentile exposure. Values are from Table 3.

Table 8b. Drinking Water Levels of Comparison for Acute Dietary Exposure w 0.15x Reduction Factor						
Population Subgroup	Acute PAD (mg/kg/day)	Food Exposure at the 99.9th percentile* (mg/kg/day)	Max. Water Exposure (mg/kg/day)	DWLOC _{acute} (ug/L)	Surface Water (ug/L) max.	Ground Water (ug/L)
US Population	0.017	0.0025	0.0145	509	98	0.03
All Infants	0.017	0.0045	0.0125	125	98	0.03
Children 1-6	0.017	0.0097	0.0073	73	98	0.03
Children 7-12	0.017	0.0036	0.0134	134	98	0.03

Table 8b. Drinking Water Levels of Comparison for Acute Dietary Exposure w 0.15x Reduction Factor

Population Subgroup	Acute PAD (mg/kg/day)	Food Exposure at the 99.9th percentile ^a (mg/kg/day)	Max. Water Exposure (mg/kg/day)	DWLOC _{acute} (ug/L)	Surface Water (ug/L) max.	Ground Water (ug/L)
Females 13-50	0.017	0.0017	0.0145	457	98	0.03
Males 13-19	0.017	0.0012	0.0158	552	98	0.03
Males 20+	0.017	0.0016	0.0154	540	98	0.03
Seniors 55+	0.017	0.0018	0.0152	533	98	0.03

(a) 99.9th percentile exposure. Values are from Table 4.

5.2 Short-Term Risk

The short-term aggregate risk estimate includes chronic (average) dietary (food and water) from ziram uses, and short-term non-occupational exposures (i.e., residential uses). No short term residential oral exposure is expected to occur. Short term dermal and inhalation exposure are possible for the homeowner as mixer/loader/applicator for ziram use on ornamentals as a rabbit repellent. Since the short term dermal and inhalation MOEs were obtained from an oral study, the dermal and inhalation exposure can be added to the average dietary (food) exposure from ziram uses. The short term DWLOC can be calculated to account for potential drinking water exposure. The short term DWLOC is compared to the chronic (average) EEC to account for potential drinking water exposure.

Negligible postapplication exposures for both children and adults are expected due to low vapor pressure and low dermal contact potential to ziram treated sites and therefore, a post application risk assessment is not necessary at this time.

5.2.1 Aggregate Short-Term Risk Assessment

The residential short-term dermal and inhalation exposures to individuals exposed to paint while using an airless sprayer alone is of concern. Therefore, no aggregate assessment for average daily dietary, short-term residential dermal and inhalation exposures was conducted. Also no DWLOC_{short-term}s were calculated.

An aggregate risk assessment for average daily dietary, short-term residential dermal and inhalation exposures of homeowners to Rabbit Scat or residential painters to paint from use of paint brush was conducted. The aggregate risk estimates indicate that risks from use of Rabbit Scat or paint (using paint brush) are not of concern.

5.2.2 Short-Term DWLOC Calculation

The calculated short term DWLOCs are presented in Table #s 9a and b. The chronic EECs are below the calculated short-term DWLOCs and therefore, aggregate risk from use of Rabbit Scat or exterior latex paint using paint brush are not of concern.

5.3 Intermediate-Term Risk

No intermediate term residential exposure is expected to occur.

5.3.1 Aggregate Intermediate-Term Risk Assessment

Not applicable

5.3.2 Intermediate-Term DWLOC Calculations

Not applicable

5.4 Chronic Risk

The chronic aggregate risk assessment for ziram addresses exposure from food and drinking water. No chronic residential exposure is expected to occur.

5.4.1 Aggregate Chronic Risk Assessment

No monitoring data for ziram residues in ground and surface water are available for estimating environmental concentrations (EECs) for the aggregate dietary (food and water) risk assessment. Therefore, computer modeling was used to estimate surface (PRZM 3.12 and EXAMS 2.97.7) and ground (SCI-GROW) water concentrations expected from normal agricultural use. These model estimates were compared to human drinking water levels of concern (DWLOCs), the theoretical concentration of pesticide in drinking water that would be an acceptable upper limit in light of the aggregate exposure to that pesticide from other sources (food and residential use). HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

Aggregate chronic risks resulting from chronic exposure to ziram via dietary (food and drinking water) exposures were assessed (given the current use patterns, no chronic residential exposure scenarios are anticipated). According to the water models, the ziram drinking water residue contribution to the chronic aggregate risk is not expected to be significant. As noted previously, the chronic food-source risks were estimated to be $\leq 28\%$ of the cPAD.

Table 9a. DWLOC/Aggregate Risk Short-Term and Aggregate Risk and DWLOC Calculations (Inhalation/Oral/Dermal Endpoints and NOAELs the Same)										
Population	NOAEL mg/kg/day	Target MOE ¹	Max Exposure ² mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure ³ mg/kg/day	Aggregate MOE (food and residential) ⁴	Max Water Exposure ⁵ mg/kg/day	Ground Water EEC ⁶ (µg/L)	Surface Water EEC ⁶ (µg/L)	Short- Term DWLOC ⁷ (µg/L)
Homeowners/ loading/apply-ing Rabbit Scat as a dust	7.5	300	0.025	0.000324	0.0052	1358	0.0195	0.03	4	680

¹The basis for the target MOE (include the standard inter- and intra- species safety factors totaling 100, as well as additional 3x uncertainty factors/safety factors as appropriate.)

² Maximum Exposure (mg/kg/day) = NOAEL/Target MOE (300)

³ Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure] = 0.0052 mg/kg/day (from Table 5a)

⁴ Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]; 0.000331 (Table 10)+ 0.0052= 0.005531; 7.5/0.005531 = 1356

⁵ Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure); 7.5 mg/kg/day÷300 - 0.00553 mg/kg/day= 0.0195 mg/kg/day

⁶ The crop producing the highest level was used.

⁷ DWLOC(µg/L) = $\frac{\text{maximum water exposure (mg/kg/day)} \times \text{body weight (70 kg)}}{[\text{water consumption (2 L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$

Table 9b. DWLOC/Aggregate Risk										
Short-Term and Aggregate Risk and DWLOC Calculations (Inhalation/Oral/Dermal Endpoints and NOAELs the Same)										
Population	NOAEL mg/kg/day	Target MOE ¹	Max Exposure ² mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure ³ mg/kg/day	Aggregate MOE (food and residential) ⁴	Max Water Exposure ⁵ mg/kg/day	Ground Water EEC ⁶ (µg/L)	Surface Water EEC ⁶ (µg/L)	Short- Term DWLOC ⁷ (µg/L)
Residential painters/paint brush	7.5	300	0.025	0.000324	0.0213	347	0.0034	0.03	4	120

¹The basis for the target MOE (include the standard inter- and intra- species safety factors totaling 100, as well as additional 3x uncertainty factors/safety factors as appropriate.)

² Maximum Exposure (mg/kg/day) = NOAEL/Target MOE (300)

³ Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure] = 0.0213 mg/kg/day (from Table 6)

⁴ Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]; 0.000331 (Table 10) + 0.0213= 0.0213; 7.5/0.0216= 352

⁵ Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure) .0034 mg/kg/day (7.5 mg/kg/day ÷ 300 - 0.0250 mg/kg/day).

⁶ The crop producing the highest level was used.

⁷ DWLOC(µg/L) = [maximum water exposure (mg/kg/day) x body weight (70 kg)] / [water consumption (2 L) x 10⁻³ mg/µg]

5.4.2 Chronic DWLOC Calculations

For chronic drinking water exposure, the DWLOC_{chronic} was calculated based on the chronic dietary (food) exposure and default body weights and water consumption. There was no chronic residential exposure. The EECs for surface water (PRZM/EXAM) and groundwater (SCI-GROW) were less than the chronic DWLOCs, indicating that chronic exposure to ziram in food and water is less than HED's level of concern (Table #10). The Agency's default body weights and water consumption used to calculate DWLOCs are as follows: 70 kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (infant). To calculate the chronic DWLOC, the chronic dietary food exposure was subtracted from the chronic PAD as shown in the following equation:

$$\text{DWLOC}_{\text{chronic}} = \frac{[\text{chronic water exposure (mg/kg/day)} \times (\text{body weight})]}{[\text{Water consumption (L)} \times 10^{-3} \text{ mg/}\mu\text{g}]}$$

Where Chronic water exposure (mg/kg/day) = cPAD-Food Exposure (mg/kg/day)

Table 10. Drinking Water Levels of Comparison for Chronic Dietary Exposure						
Population Subgroup	Chronic PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Max. Water Exposure (mg/kg/day)	DWLOC _{chronic} (ug/L)	Surface Water (ug/L)	Ground Water (ug/L)
US Population	0.005	0.0003	0.0047	164	1.98	0.03
All Infants	0.005	0.0014	0.0036	36	1.98	0.03
Children 1-6	0.005	0.0009	0.0041	41	1.98	0.03
Children 7-12	0.005	0.00067	0.0044	44	1.98	0.03
Females 13-50	0.005	0.0002	0.0048	144	1.98	0.03
Males 13-19	0.005	0.0002	0.0048	169	1.98	0.03
Males 20+	0.005	0.0002	0.0048	168	1.98	0.03
Seniors 55+	0.005	0.0003	0.0047	165	1.98	0.03

5.5 Cancer Risk

Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

6.0 Cumulative

The Food Quality Protection Act (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this reregistration review for ziram because HED has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of ziram. For purposes of this reregistration decision, EPA has assumed that ziram does not have a common mechanism of toxicity with other substances.

On this basis, the registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether ziram shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for ziram need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with ziram, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at:

http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf

In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the *"Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity"* (64 FR 5795-5796, February 5, 1999).

7.0 Occupational Exposure/Risk Pathway

Occupational exposure to ziram may occur from agricultural, ornamentals and antimicrobial uses. Occupational exposure scenarios can be described as short term (1 to 30 days), intermediate term (30 days to six months), and long term or chronic (six months to life-time). The antimicrobial and agricultural/ornamental uses are believed to be of a short- to intermediate-term duration. The toxicology

endpoints for the short- and intermediate-term dermal and inhalation exposures are based on the same effects, and therefore, the risk estimates are combined.

Handler exposures are expected from mixing/loading and applying ziram in agricultural, ornamentals and commercial/industrial settings. Handler and postapplication antimicrobial exposures are defined by the Antimicrobial Division as “*primary*” and “*secondary*” handlers. The primary handlers are defined by EPA as those individuals exposed to the formulated product (e.g., adding the ziram-containing product, Vancide MZ-96 formulated as a wettable powder, into vats of paint during its manufacturing). The secondary handlers are defined by EPA as those individuals exposed to the active ingredient as a direct result of its incorporation into an end use product (e.g., commercial painters applying ziram-treated exterior latex paint that in itself is not a registered product). Handler risks are calculated for potential exposures to dry flowable, wettable powder and liquid formulations. Although typical application rates were identified by the registrant, only the maximum rates are assessed because they do not present a risk of concern for handlers, except for commercial painters. The Agency considers the ziram occupational handler exposure estimates to be the best available with current data and methodologies.

Postapplication exposures in industrial settings are expected to be minimal. Foliar applications of ziram are expected to result in postapplication exposures to workers reentering treated fields and postapplication studies containing DFR data are available. Activity-specific transfer coefficients have been developed by the Agricultural Reentry Task Force (ARTF). These proprietary activity-specific transfer coefficients are used to estimate postapplication risks to those individuals reentering ziram treated sites (i.e., HED Exposure SAC Policy 3.1: *Agricultural Transfer Coefficients* dated August 7, 2000).

The Agency has conducted occupational risk estimates using surrogate data for loading powder formulations from the Chemical Manufacturers Association (CMA) antimicrobial exposure study (DP Barcode D247642), the Pesticide Handlers Exposure Database (PHED, version 1.1), dislodgeable foliar residue (DFR) data for apples and grapes in conjunction with HED standard values for transfer coefficients based on ARTF data as well as the toxicological endpoints chosen by the HIARC. For details regarding the assumptions and uncertainties identified during the handler exposure assessments, refer to HED’s Occupational and Residential Exposure assessment document (9/12/01; D 276788). **Note: the quantitative cancer assessment provided in the ORE document is no longer applicable because the cancer classification has been revised.**

7.1 Handler Exposure from Antimicrobial Use

Vancide MZ-96 (EPA Reg. No. 1965-79) is an industrial preservative containing 96 percent ziram as a wettable powder formulation. The product is incorporated as a preservative additive at 0.185 to 0.5 percent during the initial phase of the manufacturing process in adhesives, caulks, sealants, and wallboard and 1 to 3 percent as a mold inhibitor for exterior latex paint. Based on the label directions, ziram is added to dry starch and synthetic latex adhesives because they are “*subject to bacterial degradation when water is added by the end user*”. It is added to dried films because they are “*subject to defacement by mold and mildew including wall and ceiling textures, wallpaper paste, wallboard joint compounds, spackles, wood fillers, caulks and sealants*”. Finally, ziram is added to paints as an in-can preservative. Although there is potential exposure during the application of the other treated materials (e.g., caulks and sealants), they are not included because no data are available to assess the uses. It is HED’s professional judgement that the painting scenarios represent the high end exposures for ziram antimicrobial secondary uses. For the discussion of uncertainties refer to the HED’s Occupational and Residential Exposure assessment document (9/12/01; D276788). **Note: the quantitative cancer assessment provided in the ORE document is no longer applicable because the cancer classification has been revised.**

According to the manufacturer, the antimicrobial users mix commercial products with ziram every other week at a frequency of 5 days per week (Memorandum dated August 16, 2001 from Frank Flynn Vanderbilt Co. to Tim Leighton U.S. EPA). This type of intermittent exposure frequency is not considered a chronic exposure scenario for ziram (i.e., greater than 180 days) because ziram is not used continuously for at least 180 days and urinary and fecal excretion of ziram is nearly complete within 72 hours at low-dose groups and within 96 hours within high-dose groups in the rat metabolism study (HED Doc. No. 014277).

The MOE results of the antimicrobial assessment are presented above in Table #11. For the general preservative use, the short- and intermediate-term total MOEs for the primary handlers wearing long pants, long sleeved shirts, chemical resistant gloves, and a dust/mist respirator at the 0.5 percent Vancide concentration range from a high of 670,000 for the product with the lowest density and percent solids (i.e., CBP Patch N Paint at 3 pounds per gallon with a 7.3 percent solid) and as low as 1,100 for the product with the highest density and percent solids (i.e., texture coating 16 pounds per gallon with 84 percent solids). The intermediate-term total MOEs for the handlers adding ziram to paint during the manufacturing process at the maximum Vancide concentration (i.e., 0.5 percent) are 2,500 for 100 gallon paint batches and 250 for 1,000 gallon paint batches. Although the MOEs are sufficiently above the target MOE of 100 to remove some of the PPE, the CMA data do not accommodate exposure estimates for lower levels of PPE. The short- and intermediate-term total MOEs for the commercial painters while wearing long pants and long sleeved shirts are 30 for commercial painters using airless sprayers and 170 for commercial painters using paint brushes. No mitigation measures are available for the secondary exposures because the individuals that are being exposed to paint containing ziram are exposed to products with no pesticide labels (i.e., in-can preservative use). Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

7.2 Postapplication Exposure from Antimicrobial Use

Postapplication dermal and inhalation exposures may occur in the industrial settings around open vats of processing material while maintaining industrial equipment. No postapplication exposure data have been submitted to determine the extent of postapplication exposures in the industrial settings. Nonetheless, inhalation exposures are expected to be minimal because of the low vapor pressure of ziram ($1.4\text{E-}7$ mmHg at 25C) and aerosols are not expected. Dermal postapplication exposures are expected to be lower than when handling/loading the 96 percent formulated product. Postapplication inhalation and dermal exposures in the residential settings, as a result of commercial applications of products such as paints, are also expected to be minimal because of the low vapor pressure of ziram and low dermal contact potential to the treated surfaces and/or adhesives. Therefore, postapplication exposures in the residential (as a result of commercial applications) and industrial settings are expected to be minimal and not of concern. For further details refer to HED's Occupational and Residential Exposure assessment document (9/12/01; D276788). **Note: the quantitative cancer assessment provided in the ORE document is no longer applicable because the cancer classification has been revised.**

Table 11. Short- and Intermediate-term Antimicrobial Uses of Ziram and MOEs.

Exposure Scenario	Population Targeted	Clothing Attire	Dermal Unit Exposure (mg/lb ai) ^a	Inhalation Unit Exposure (µg/lb ai) ^b	Appl. Rate ^c (lb ai/gal)	Amount Treated ^d	Absorbed Dermal Dose (mg/kg/day) ^e	Dermal MOE	Inhalation Dose (mg/kg/day) ^f	Inhalation MOE	Total MOE ^h
Primary Handlers: Short- and Intermediate-term Exposure Duration											
Loaders of WP for General Preservatives	Occupational	Open pour, long pants, long-sleeved shirt, chemical resistant gloves, and a 5-fold PF dust/mist type respirator	0.466	2.5	0.0011 min rate	100 gal	7.3E-6	1E+6	3.9E-6	1.9E+6	670,000
						1,000 gal	7.3E-5	1E+5	3.9E-5	1.9E+5	67,000
					0.065 max rate	100 gal	0.00043	17,000	0.00023	32,000	11,000
						1,000 gal	0.0043	1,700	0.0023	3,200	1,100
Loaders of WP for Paint Manufacturers	Occupational		0.466	2.5	0.29 max rate	100 gallons	0.0019	3,900	0.0010	7,200	2,500
						1,000 gal	0.019	390	0.010	720	250
Secondary Handlers: Short- and Intermediate-term Commercial Exposure Durations											
Airless Sprayers	Commercial	Long pants, long sleeved shirt	38	830	0.29 max rate	50 gallons	0.079	95	0.17	44	30
Paint Brush	Commercial	Long pants, long sleeved shirt	180	280	0.29 max rate	5 gallons	0.037	200	0.0058	1,300	170

^{a,b} Dermal and inhalation unit exposures are from CMA study and PHED V1.1.

^c Application rates are based on the Vancide MZ 96 label (EPA Reg. No.1965-79) along with density and % solid information from Vanderbilt Co.

^d Amount treated is based on assumptions from EPA's Antimicrobial Division and HED's Residential SOPs.

^e Abs. dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai/gallon) * gallons handled / Body weight (70 kg).

^f MOE = NOAEL (mg/kg/day) / Daily Dose [Where short-and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. Target MOE is 100 for occupational/ commercial and 300 for residential.

^g Inhalation dose (mg/kg/day) = [unit exposure (µg/lb ai) * 0.001 mg/µg unit conversion * max appl rate (lb ai/gal) * gallons handled * 1 inhalation absorption] / Body weight (70 kg).

^h Total MOE (short- and intermediate-term duration) = 1/((1/dermal MOE) + (1/inhalation MOE)).

7.3 Handler Exposures for Agricultural Uses

The results of the agricultural occupational handler assessments (see Table #s 12-15; pg 29) from agricultural use indicate that for the *dry flowable formulation* all of the potential exposure scenarios provide dermal and inhalation MOE(s) greater than or equal to 100 at the baseline clothing attire of long pants, long sleeved shirts, no gloves, and no respirator while using open systems. However, based on the acute inhalation toxicity category II classification and the review of the ziram incident reports (DP Barcod D276936), a dust/mist respirator is recommended to protect against inhalation exposure. Although the incident data do not indicate direct respiratory illness, the respiratory effects are reported as part of the “systemic” and “combination” categories. Because most current labels require a dust/mist respirator, incidents may increase if the respirator were to be removed. The use of a respirator is consistent with some of the current dry flowable labels (EPA Reg. Nos. 4581-140 and 45728-12), but the Drexel Ziram 76 label (EPA Reg. No. 19713-68) does not require a respirator. For the *liquid formulation*, for the mixer/loaders to achieve MOEs of 100 for all uses at both the short- and intermediate-term exposure durations that minimum PPE clothing attire be required (i.e., long pants, long sleeved shirts, chemical resistant gloves, and a dust/mist respirator while using open systems). This is consistent with the current label except for the need in some scenarios to add a dust/mist respirator (EPA Reg. No. 19713-270). Finally, for the *wettable powder formulation* risks indicate that in order for the mixer/loaders to achieve MOEs of 100 for all uses at both the short- and intermediate-term durations that the wettable powder be packaged in water soluble packets (clothing attire of long pants, long sleeved shirts, chemical resistant gloves, and no respirator). The current wettable powder formulation is not packaged in water soluble packets (EPA Reg. No. 34704-471). Based on the CARC's revised cancer classification of ziram to the category “Suggestive of carcinogenicity to humans,” a

quantitative assessment of human carcinogenic risk is not required.

7.4 Postapplication Exposure for Agricultural Uses

Several levels of postapplication exposure activities have been identified ranging from “low” activities such as weeding and scouting in immature plants to very high activities such as harvesting or thinning fruit from trees. The short- and intermediate-term postapplication assessments indicate that the potential restricted entry interval (REI) (i.e., the day after treatment that the MOEs reaches 100), based on the toxicity of the active ingredient, is 0 days for all crops and all activities. Based on the CARC’s revised cancer classification of ziram to the category “Suggestive of carcinogenicity to humans,” a quantitative assessment of human carcinogenic risk is not required. Although MOEs of 100 are achieved for all crops and all activities on day 0, ziram is an acute Tox I category for eye irritation, and therefore, the REI will be a minimum of 48 hours.

8.0 Conclusion

In conclusion, the Agency’s exposure estimates presented are conservative and the data indicate that washing can reduce residues by at least 85% or more. Thus, the risk estimates can be further refined with additional washing study data which are therefore required as confirmatory data. The Agency finds that the estimated acute dietary (food) exposures (without applying reduction factor from washing study) exceed HED’s level of concern for All Infants, and Children (1-6 years old) at the 99.9th percentile. However, after applying the reduction factor (0.15X) from the peach washing study to all commodities (except nuts and berries) the maximum dietary risk estimates are below HED’s level of concern for all population subgroups.

The estimated chronic dietary risks are below HED’s level of concern for all population subgroups without application of reduction factor. Based on the CARC’s revised cancer classification of ziram to the category “Suggestive of carcinogenicity to humans,” a quantitative assessment of human carcinogenic risk is not required. The EECs for surface water were greater than the acute DWLOCs, for three population subgroups (infants, children 1-6, and children 7-12) indicating that one-day maximum exposure to ziram in surface water plus one-day exposures to ziram in food (without applying reduction factor from washing study) exceeds HED’s level of concern at the 99.9th percentile of exposure for these population subgroups. Surface water EECs were less than the acute DWLOCs (without washing) for all other population subgroups. After applying the reduction factor from the peach washing study, the EECs for surface water were greater than the acute DWLOCs, for 1-6 year child population subgroup only. The EECs for surface water (PRZM/EXAM) and groundwater (SCI-GROW) were less than the chronic DWLOCs, indicating that chronic exposure to ziram in food and water is less than HED’s level of concern. The aggregate chronic dietary (food + water) risk estimates do not exceed HED’s level of concern.

The registered non-occupational dermal and inhalation exposures of residential handlers to ziram do not exceed HED’s level of concern. The postapplication exposures for both adults and children from residential use are expected to be minimal because of the nature of the residential application (foliar applications to outdoor ornamentals). Therefore, a post application risk assessment is not necessary at this time.

The short-term dermal and inhalation exposures of residential painters from ziram-treated in-can preservative use (while using airless sprayer) are of concern. Based on the CARC’s revised cancer classification of ziram to the category “Suggestive of carcinogenicity to humans,” a quantitative assessment of human carcinogenic risk is not required. Postapplication dermal and inhalation exposure in residential settings from the antimicrobial uses (e.g., exterior latex paint, caulks, adhesives) are expected to be negligible due to low vapor pressure of ziram and low dermal contact potential to treated surfaces. Therefore, dermal and inhalation exposure risk was not estimated.

An aggregate assessment for average daily dietary, short-term residential dermal and inhalation exposures of

homeowners to Rabbit Scat or residential painters to paint from use of paint brush indicates that the chronic EECs are below the calculated short-term DWLOCs and therefore, aggregate risks from use of Rabbit Scat or use of paint brush are not of concern.

In addition to agricultural handlers and postapplication, antimicrobial primary handlers short- and intermediate-term exposure estimates, associated with the dermal and inhalation exposures to ziram do not exceed HED's level of concern with the proper mitigation measures detailed in the document. However, short- and intermediate-term dermal and inhalation exposures to commercial painters from ziram-treated in-can preservative use are of concern. Based on the CARC's revised cancer classification of ziram to the category "Suggestive of carcinogenicity to humans," a quantitative assessment of human carcinogenic risk is not required.

9.0 Data Needs/Label Requirements

Additional data requirements have been identified in the attached Science Chapters and are summarized here.

Toxicology Data for OPPTS Guidelines:

- A metabolite identification study in rats. (GLN 870.7485).
- A 28-day inhalation study (GLN 870.3465).
- Morphometric analyses of brain tissues and statistical analyses of neurobehavioral data in the Developmental neurotoxicity study (GLN 870.6300).

Residue Chemistry Data for OPPTS Guidelines

- The nature of the residue in plants and animals is not adequately understood (GLN 860.1300).
- Tolerances are needed for ziram residues in livestock commodities and processed food/feed commodities.
- Additional data are required to ascertain the adequacy of the established tolerances for blackberries; blueberries; grapes; and tomatoes (GLN 860.1500).
- Additional residue reduction studies including washing and processing studies required for orchard fruits to refine the risk assessment. Cooking data are suggested (GLN 171-5).
- Additional solubility studies are required to resolve inconsistencies in the solubility data for the three technicals (GLN 830.7840).

Table 12 Short - and Intermediate-Term Baseline Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).										
Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Dry Flowables for Aerial application (1)	0.066	0.77	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.020	370	0.023	320	170
Dry Flowables for Aerial application (2)	0.066	0.77	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.025	300	0.029	260	140
Dry Flowables for Airblast application (3)	0.066	0.77	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0023	3300	0.0027	2800	1500

Table 12 Short - and Intermediate-Term Baseline Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).										
Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Dry Flowables for Airblast application (4)	0.066	0.77	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0029	2600	0.0033	2200	1200
Dry Flowables for Groundboom application (5)	0.066	0.77	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.0023	3300	0.0027	2800	1500
Dry Flowables for High-Pressure HandWand application (6)	0.066	0.77	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.00019	40000	0.00022	34000	18000
Mixing/Loading Liquids for Aerial application (7)	2.9	1.2	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.88	9	0.036	210	8.2
Mixing/Loading Liquids for Aerial application (8)	2.9	1.2	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	1.1	7	0.046	160	6.5
Mixing/Loading Liquids for Airblast application (9)	2.9	1.2	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.10	74	0.0042	1800	71
Mixing/Loading Liquids for Airblast application (10)	2.9	1.2	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.13	60	0.0052	1400	57
Mixing/Loading Liquids for Groundboom application (11)	2.9	1.2	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.10	74	0.0042	1800	71
Mixing/Loading Liquids for High-Pressure HandWand application (12)	2.9	1.2	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.0083	910	0.00034	22000	870
Wettable Powders for Aerial application (13)	3.7	43	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	1.1	7	1.3	6	3.1
Wettable Powders for Aerial application (14)	3.7	43	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	1.4	5	1.6	5	2.5
Wettable Powders for Airblast application (15)	3.7	43	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.13	58	0.15	50	27
Wettable Powders for Airblast application (16)	3.7	43	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.16	47	0.19	40	22
Wettable Powders for Groundboom application (17)	3.7	43	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.13	58	0.15	50	27
Wettable Powders for High-Pressure HandWand application (18)	3.7	43	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.011	710	0.012	610	330
Applicator										

Table 12 Short- and Intermediate-Term Baseline Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).										
Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Sprays for Aerial application (19)	No Data	No Data	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	NoData
Sprays for Aerial application (20)	No Data	No Data	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	NoData
Sprays for Airblast application (21)	0.36	4.5	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.013	600	0.016	480	270
Sprays for Airblast application (22)	0.36	4.5	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.016	480	0.020	380	210
Sprays for Groundboom application (23)	0.014	0.74	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00049	15000	0.0026	2900	2500
Sprays for High-Pressure HandWand application (24)	1.8	79	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.0051	1500	0.023	330	270
Flagger										
Flagging for Sprays application (25)	0.011	0.35	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0042	1800	0.013	560	430

a,b Baseline dermal and inhalation unit exposures represent long pants, long sleeved shirts, no gloves, and no respirator. Values are reported in the PHED Surrogate Exposure Guide dated August 1998.

c Crops treated with ziram are presented in Table 3.

d Application rates are based on Ziram 76DF (EPA Reg. No. 4581-140) along with the information obtained during the SMART meeting. In addition, a Ziram 76W wettable powder label (EPA Reg Nos. 134704-471) and a Ziram 4L liquid label exist (EPA Reg. No. 19713-270). Amount treated is based on the area or gallons that can be reasonably applied in a single day (standard EPA/OPP/HED values).

f Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 Dermal absorption * Appl. rate (lb ai/acre or lb ai/gallon) * Acres or gallons] / Body weight (70 kg).

g MOE = NOAEL (mg/kg/day) / Daily Dose [Where short- and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day.] Target MOE is 100.

h Inhalation dose (mg/kg/day) = [unit exposure (ug/lb ai) * 0.001 mg/ug unit conversion * max appl rate (lb ai/A or lb ai/gal) * area treated (acres or gal) * 100 percent inhalation absorption] / Body weight (70 kg).

i Total MOE = 1/((1/dermal MOE) + (1/inhalation MOE)).

Table 13 Short- and Intermediate-Term Minimal PPE Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h)										
Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Mixer/Loader										
Dry Flowables for Aerial application (1)	0.066	0.15	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.020	370	0.0046	1600	300
Dry Flowables for Aerial application (2)	0.066	0.15	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.025	300	0.0057	1300	240
Dry Flowables for Airblast application (3)	0.066	0.15	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0023	3300	0.00052	14000	2700
Dry Flowables for Airblast application (4)	0.066	0.15	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0029	2600	0.00065	12000	2100

Table 13 Short- and Intermediate-Term Minimal PPE Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Dry Flowables for Groundboom application (5)	0.066	0.15	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.0023	3300	0.00052	14000	2700
Dry Flowables for High-Pressure HandWand application (6)	0.066	0.15	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.00019	40000	0.000043	180000	32000
Mixing/Loading Liquids for Aerial application (7)	0.023	0.24	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.0070	1100	0.0073	1000	520
Mixing/Loading Liquids for Aerial application (8)	0.023	0.24	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0087	860	0.0091	820	420
Mixing/Loading Liquids for Airblast application (9)	0.023	0.24	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.00080	9400	0.00083	9000	4600
Mixing/Loading Liquids for Airblast application (10)	0.023	0.24	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.000100	7500	0.0010	7200	3700
Mixing/Loading Liquids for Groundboom application (11)	0.023	0.24	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00080	9400	0.00083	9000	4600
Mixing/Loading Liquids for High-Pressure HandWand application (12)	0.023	0.24	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.000066	110000	0.000069	110000	56000
Wettable Powders for Aerial application (13)	0.17	8.6	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.052	150	0.26	29	24
Wettable Powders for Aerial application (14)	0.17	8.6	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.065	120	0.33	23	19
Wettable Powders for Airblast application (15)	0.17	8.6	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0059	1300	0.030	250	210
Wettable Powders for Airblast application (16)	0.17	8.6	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0074	1000	0.037	200	170
Wettable Powders for Groundboom application (17)	0.17	8.6	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.0059	1300	0.030	250	210
Wettable Powders for High-Pressure HandWand application (18)	0.17	8.6	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.00049	15000	0.0025	3100	2500
Applicator										
Sprays for Aerial application (19)	No Data	No Data	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	No Data

Table 13 Short- and Intermediate-Term Minimal PPE Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (µg/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Sprays for Aerial application (20)	No Data	No Data	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	No Data
Sprays for Airblast application (21)	0.24	0.9	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0083	900	0.0031	2400	650
Sprays for Airblast application (22)	0.24	0.9	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.010	720	0.0039	1900	520
Sprays for Groundboom application (23)	0.014	0.15	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00049	15000	0.00052	14000	7400
Sprays for High-Pressure HandWand application (24)	0.64	16	Ornament als	0.02 lb ai per gallon	1000 Gallons per day	0.0018	4100	0.0046	1600	1200
Flagger										
Flagging for Sprays application (25)	0.01	0.07	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0038	2000	0.0027	2800	1200

a,b Minimum PPE dermal and inhalation unit exposures represent long pants, long sleeved shirts, chemical resistant gloves, and dust/mist respirator (5-fold PF). Values are reported in the PHED Surrogate Exposure Guide dated August 1998.

c Crops treated with ziram are presented in Table 3.

d Application rates are based on Ziram 76DF (EPA Reg. No. 4581-140) along with the information obtained during the SMART meeting. In addition, a Ziram 76W wettable powder label (EPA Reg Nos. 134704-471) and a Ziram 4L liquid label exist (EPA Reg. No. 19713-270). Amount treated is based on the area or gallons that can be reasonably applied in a single day (standard EPA/OPP/HED values).

e Absorbed Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai/acre or lb ai/gallon) * Acres or gallons] / Body weight (70 kg).

f MOE = NOAEL (mg/kg/day) / Daily Dose [Where short- and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. The target MOE is 100.

g Inhalation dose (mg/kg/day) = [unit exposure (µg/lb ai) * 0.001 mg/µg unit conversion * max appl rate (lb ai/A or lb ai/gal) * area treated (acres or gal) * 100 percent inhalation absorption] / Body weight (70 kg).

h Total MOE = 1/((1/dermal MOE) + (1/inhalation MOE)).

Table 14. Short- and Intermediate-Term Max PPE Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Mixer/Loader										
Dry Flowables for Aerial application (1)	0.047	0.077	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.014	530	0.0023	3200	450
Dry Flowables for Aerial application (2)	0.047	0.077	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.018	420	0.0029	2600	360
Dry Flowables for Airblast application (3)	0.047	0.077	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0016	4600	0.00027	28000	3900
Dry Flowables for Airblast application (4)	0.047	0.077	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0020	3700	0.00033	22000	3200
Dry Flowables for Groundboom application (5)	0.047	0.077	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.0016	4600	0.00027	28000	3900
Dry Flowables for High-Pressure HandWand application (6)	0.047	0.077	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.00013	56000	0.000022	340000	48000
-Mixing/Loading Liquids for Aerial application (7)	0.017	0.12	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.0052	1500	0.0036	2100	850
Mixing/Loading Liquids for Aerial application (8)	0.017	0.12	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0065	1200	0.0046	1600	680
Mixing/Loading Liquids for Airblast application (9)	0.017	0.12	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.00059	13000	0.00042	18000	7400
Mixing/Loading Liquids for Airblast application (10)	0.017	0.12	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.00074	10000	0.00052	14000	6000
Mixing/Loading Liquids for Groundboom application (11)	0.017	0.12	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00059	13000	0.00042	18000	7400
Mixing/Loading Liquids for High-Pressure HandWand application (12)	0.017	0.12	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.000049	150000	0.000034	220000	91000
Wettable Powders for Aerial application (13)	0.13	4.3	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.040	190	0.13	57	44
Wettable Powders for Aerial application (14)	0.13	4.3	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.049	150	0.16	46	35
Wettable Powders for Airblast application (15)	0.13	4.3	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0045	1700	0.015	500	390
Wettable Powders for Airblast application (16)	0.13	4.3	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0056	1300	0.019	400	310

Table 14. Short- and Intermediate-Term Max PPE Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h)

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Wettable Powders for Groundboom application (17)	0.13	4.3	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.0045	1700	0.015	500	390
Wettable Powders for High-Pressure HandWand application (18)	0.13	4.3	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.00037	20000	0.0012	6100	4700
Applicator										
Sprays for Aerial application (19)	No Data	No Data	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	No Data
Sprays for Aerial application (20)	No Data	No Data	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	No Data
Sprays for Airblast application (21)	0.22	0.45	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.0076	980	0.0016	4800	810
Sprays for Airblast application (22)	0.22	0.45	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.0096	790	0.0020	3800	650
Sprays for Groundboom application (23)	0.011	0.074	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00038	20000	0.00026	29000	12000
Sprays for High-Pressure HandWand application (24)	0.36	7.9	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.0010	7300	0.0023	3300	2300
Flagger										
Flagging for Sprays application (25)	0.01	0.035	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0038	2000	0.0013	5600	1500

a,b Maximum PPE dermal and inhalation unit exposures represent coveralls over long pants, long sleeved shirts, chemical resistant gloves, and an O/V respirator or equivalent 10-fold PF. Values are reported in the PHED Surrogate Exposure Guide, August 1998.

c Crops treated with ziram are presented in Table 3.

d Application rates are based on Ziram 76DF (EPA Reg. No. 4581-140) along with the information obtained during the SMART meeting. In addition, a Ziram 76W wettable powder label (EPA Reg Nos. 134704-471) and a Ziram 4L liquid label exist (EPA Reg. No. 19713-270).

e Amount treated is based on the area or gallons that can be reasonably applied in a single day (standard EPA/OPP/HED values).

f Absorbed Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai/acre or lb ai/gallon) * Acres or gallons] / Body weight (70 kg).

g MOE = NOAEL (mg/kg/day) / Daily Dose [Where short- and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. The target MOE is 100.

h Inhalation dose (mg/kg/day) = [unit exposure (ug/lb ai) * 0.001 mg/ug unit conversion * max appl rate (lb ai/A or lb ai/gal) * area treated (acres or gal) * 100 percent inhalation absorption] / Body weight (70 kg).

i Total MOE = 1/((1/dermal MOE) + (1/inhalation MOE)).

Table 15 Short- and Intermediate-Term Engineering Control Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Mixer/Loader										

Table 15 Short- and Intermediate-Term Engineering Control Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (Ug/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Dry Flowables for Aerial application (1)	No Data	No Data	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	N/A
Dry Flowables for Aerial application (2)	No Data	No Data	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	No Data	No Data	No Data	No Data	
Dry Flowables for Airblast application (3)	No Data	No Data	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	No Data	No Data	No Data	No Data	
Dry Flowables for Airblast application (4)	No Data	No Data	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	No Data	No Data	No Data	No Data	
Dry Flowables for Groundboom application (5)	No Data	No Data	Tomatoes	3.04 lb ai per acre	80 Acres per day	No Data	No Data	No Data	No Data	
Dry Flowables for High-Pressure HandWand application (6)	No Data	No Data	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	No Data	No Data	No Data	No Data	
Mixing/Loading Liquids for Aerial application (7)	0.0086	0.083	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.0026	2900	0.0025	3000	1500
Mixing/Loading Liquids for Aerial application (8)	0.0086	0.083	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0033	2300	0.0032	2400	1200
Mixing/Loading Liquids for Airblast application (9)	0.0086	0.083	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.00030	25000	0.00029	26000	13000
Mixing/Loading Liquids for Airblast application (10)	0.0086	0.083	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.00037	20000	0.00036	21000	10000
Mixing/Loading Liquids for Groundboom application (11)	0.0086	0.083	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00030	25000	0.00029	26000	13000
Mixing/Loading Liquids for High-Pressure HandWand application (12)	0.0086	0.083	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.000025	310000	0.000024	320000	160000
Wettable Powders for Aerial application (13)	0.0098	0.24	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.0030	2500	0.0073	1000	730
Wettable Powders for Aerial application (14)	0.0098	0.24	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0037	2000	0.0091	820	580
Wettable Powders for Airblast application (15)	0.0098	0.24	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.00034	22000	0.00083	9000	6400
Wettable Powders for Airblast application (16)	0.0098	0.24	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.00043	18000	0.0010	7200	5100
Wettable Powders for Groundboom application (17)	0.0098	0.24	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00034	22000	0.00083	9000	6400

Table 15 Short- and Intermediate-Term Engineering Control Dermal, Inhalation, and Total MOEs for Ziram (a, b, c, d, e, f, g, h).

Exposure Scenario (Scenario #)	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (µg/lb ai)	Crop	Application Rate	Amount Treated	Dermal Dose (mg/kg/day)	Dermal MOE	Inhalation Dose (mg/kg/day)	Inhalation MOE	Total MOE
Wettable Powders for High-Pressure HandWand application (18)	0.0098	0.24	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	0.000028	270000	0.000069	110000	78000
Applicator										
Sprays for Aerial application (19)	0.005	0.068	Max Tree Rate	6.08 lb ai per acre	350 Acres per day	0.0015	4900	0.0021	3600	2100
Sprays for Aerial application (20)	0.005	0.068	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.0019	3900	0.0026	2900	1700
Sprays for Airblast application (21)	0.019	0.45	Max Tree Rate	6.08 lb ai per acre	40 Acres per day	0.00066	11000	0.0016	4800	3400
Sprays for Airblast application (22)	0.019	0.45	Dormant Peaches Only	7.60 lb ai per acre	40 Acres per day	0.00083	9100	0.0020	3800	2700
Sprays for Groundboom application (23)	0.005	0.043	Tomatoes	3.04 lb ai per acre	80 Acres per day	0.00017	43000	0.00015	50000	23000
Sprays for High-Pressure HandWand application (24)	No Data	No Data	Ornamentals	0.02 lb ai per gallon	1000 Gallons per day	No Data	No Data	No Data	No Data	N/A
Flagger										
Flagging for Sprays application (25)	0.00022	0.007	Dormant Peaches Only	7.60 lb ai per acre	350 Acres per day	0.000084	90000	0.00027	28000	21000

- a,b Engineering control dermal and inhalation unit exposures represent closed systems (closed loading and enclosed cabs) while wearing long pants, long sleeved shirts, no gloves, and no respirator (except airblast applicator wearing chemical resistant gloves -- only data available). Values are reported in the PHED Surrogate Exposure Guide dated August 1998.
- c Crops treated with ziram are presented in Table 3.
- d Application rates are based on Ziram 76DF (EPA Reg. No. 4581-140) along with the information obtained during the SMART meeting. In addition, a Ziram 76W wettable powder label (EPA Reg Nos. 134704-471) and a Ziram 4L liquid label exist (EPA Reg. No. 19713-270).
- e Amount treated is based on the area or gallons that can be reasonably applied in a single day (standard EPA/OPP/HED values).
- f Absorbed Dermal dose (mg/kg/day) = [unit exposure (mg/lb ai) * 0.01 dermal absorption * Appl. rate (lb ai/acre or lb ai/gallon) * Acres or gallons] / Body weight (70 kg).
- g MOE = NOAEL (mg/kg/day) / Daily Dose [Where short- and intermediate-term dermal and inhalation NOAEL = 7.5 mg/kg/day]. The target MOE is 100.
- h Inhalation dose (mg/kg/day) = [unit exposure (µg/lb ai) * 0.001 mg/µg unit conversion * max appl rate (lb ai/A or lb ai/gal) * area treated (acres or gal) * 100 percent inhalation absorption] / Body weight (70 kg).
- i Total MOE = 1/((1/dermal MOE) + (1/inhalation MOE)).